CALIBRATION OF FLUIDIC DEVICES

CROSS-REFERENCE

This application claims the benefit of U.S. Provisional Application No. 60/678,801, filed May 9,2005 and U.S. Provisional Application No. 60/705,489, filed Aug. 5, 2005 and U.S. Provisional Application No. 60/717,192, filed Sep. 16, 2005, and U.S. Provisional Application No. 60/721,097, filed Sep. 28, 2005 which are incorporated herein by reference in their entirety.

BACKGROUND OF THE INVENTION

The discovery of a vast number of biomarkers implicated in a wide variety of biological processes and the establishment of miniaturized microfluidic systems have opened up avenues to devise methods and systems for the prediction, diagnosis and treatment of diseases in a point-of-care setting. Point-of-care testing is particularly desirable because it rapidly delivers results to medical practitioners and enables faster consultation.

Performing assays, particularly immunoassays, on microfluidic systems of patient samples requires careful, precise calibration using data gathered in parallel with the sample measurement by measuring known standards or calibrators using the same assay protocol and reagents, or data provided by a manufacturer that are specific to a particular lot of reagents and assay conditions. Generally, such manufacturer provided calibration data are associated with strict temperature and other assay related conditions. Such calibration information is critical in accurately determining the relationship between the response or output from the assay system and the analyte concentration in a sample. Errors due to mis-calibration of distributed assay systems, especially in the case of immunoassays and particularly in the case of immunoassays that do not use "excess" reagents could lead to significant errors in determining the concentration of an analyte of interest.

There is therefore a significant need for methods that would improve the calibration in hand held or disposable assay units, particularly in those units where the sample and/or reagent volumes are in the microliter and nanoliter ranges, where maintaining a controlled temperature may be impractical, where the sample may not be "clean" such that errors are caused by interfering substances, or where it is difficult to maintain the desired conditions such as temperature, reagent quality, or sample volume.

SUMMARY OF THE INVENTION

The present invention provides a method of improving the accuracy of calibrating a fluidic system. The method comprises providing a system for detecting an analyte in a bodily fluid from a subject comprising a fluidic device for providing said bodily fluid, said fluidic device having a calibration assembly and a reader assembly for detecting the presence of said analyte, measuring one or more parameters of a calibration curve associated with said fluidic device, comparing said one or more parameters with predetermined parameters associate with said fluidic device, and adjusting a signal output by the ratio of said one or more parameters and said predetermined parameters.

In one aspect of the method the predetermined parameters are parameters determined at the time the fluidic device is manufactured.

In another aspect of the method the predetermined parameters are replaced with said measured one or more parameters to be used in a calibration curve to scale a signal to determine said analyte concentration.

The present invention provides another method of improving the calibration of a fluidic system The method comprises measuring a first signal in an original sample comprising a known quantity of an analyte, measuring a second signal after spiking said original sample with a known quantity of said analyte, plotting the difference between said first and second signals against a target value, wherein said target value is a signal expected for said known quantity of said analyte, and arriving at a best fit of parameters by minimizing the sum of the square of the differences between said target value and calculated analyte values.

In one aspect of the method the sample is provided to a fluidic device, the fluidic device comprises a sample collection unit and an assay assembly, wherein said sample collection unit allows a sample of bodily fluids to react with reactants contained within said assay assembly.

The present invention further provides a method of assessing the reliability of an assay for an analyte in a bodily fluid with the use of a fluidic device. The method comprises providing a system, the system comprising a fluidic device, said fluidic device comprising a sample collection unit and an assay assembly, wherein said sample collection unit allows a sample of bodily fluid to react with reactants contained within said assay assembly, for detecting the presence of an analyte in a bodily fluid from a subject, and a reader assembly for detecting the presence of said analyte, and sensing with a sensor a change in operation parameters under which the system normally operates.

One aspect of the method further comprises improving the reliability of said assay by adjusting the operating parameters to effect normal functioning of the system.

In one aspect the sensor is associated with the fluidic device and is capable of communicating the change to the reader assembly.

In some aspects the change is a change in temperature, pressure, or the presence of moisture.

In one aspect the sensor is associated with the reader assembly and is capable of communicating said change to an external device.

One aspect of the method further comprises adjusting a calibration step of said system.

One aspect of the method further comprises wirelessly communicating said change via a handheld device.

Further provided in the present invention is a method of performing a trend analysis on the concentration of an analyte in a subject. The method comprises providing a fluidic device comprising at least one sample collection unit, an immunoassay assembly containing immunoassay reagents, a plurality of channels in fluid communication with said sample collection unit and/or said immunoassay assembly, actuating said fluidic device and directing said immunoassay reagents within said fluidic device, allowing a sample of bodily fluid of less than about 500 ul to react with said immunoassay reagents contained within said assay immunoassay assembly to yield a detectable signal indicative of the presence of said analyte in said sample, detecting said detectable signal generated from said analyte collected in said sample of bodily